Remarks

Claims 1-3, 6, and 13 remain pending in the application. Claims 14-50 have been canceled without prejudice to their prosecution in a continuing application, solely to simplify prosecution of the present application. Claims 1-3 have been limited to inhibition of DNA methyltransferase-1 and its expression. DNA methyltransferase-1 is the human DNA methyltransferase-1 identified in the specification as GenBank Accession No. X63692.

Claims 1-3, 6 and 13 remain rejected for non-enablement. Applicants respectfully traverse this rejection. In the rejection references are cited for the proposition that whether particular antisense oligonucleotides will be effective is unpredictable due to secondary structures of particular mRNAs. As a general proposition, this may be true for certain genes. However, in the case of human DNA methyltransferase-1, undue experimentation is not required. Proof of this is provided in the Declaration of Dr. Moshe Szyf provided with Applicants' reply submitted August 13, 2002 (see particularly paragraph 8). Of 8 oligonucleotides complementary to the human DNA methyltransferase-1 gene, 4 showed antisense activity. Applicants respectfully submit that this does not represent undue experimentation.

With respect to the protein effector, the invention is not a particular protein effector for human DNA methyltransferase-1, but rather the surprising finding that inhibiting expression of human DNA methyltransferase gene expression is synergistic with the inhibition of human DNA methyltransferase protein. This synergy is clearly shown in Example 6 and in Figures 19, 20A and 20B. Applicants disclose as examples of such protein effectors 5-aza-dC, 5-fluoro-2'-deoxycytidine, 5-aza-riboC, 5,6-dihydro-5-azacytidine and mechanism-based inhibitors such as those disclosed in WO97/44346 (now U.S. Patent No. 6,268,137). The nature of the protein effector should not matter, the fact is that inhibition of human DNA-methyltransferase-1 protein is synergistic with inhibition of human DNA-methyltransferase gene expression.

For the foregoing reasons, Applicants respectfully request that the rejection of claims 1-3, 6 and 13 be withdrawn.

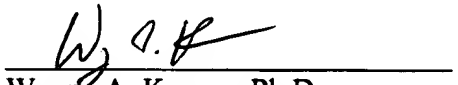
Claims 1-3, 6 and 13 remain rejected as not satisfying the written description requirement. Applicants respectfully traverse this rejection. Applicants hereby incorporate by reference the arguments made above. Moreover, as the Examiner has stated, the written description requirement can be satisfied by disclosing a working example of the claimed method. Applicants do exactly this in Example 6 and Figures 19, 20A and 20B. There is no requirement that multiple working examples be disclosed to satisfy the written description requirement. The fact is that Applicants demonstrate, by working example, that inhibition of human DNA methyltransferase-1 enzyme and inhibition of expression of the human DNA methyltransferase-1 gene is synergistic *in vivo*. Thus, one skilled in the art, reading Example 6 and examining Figures 19, 20A and 20Bwould recognize that Applicants had possession of the claimed method as of the filing date. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Claims 1-3, 6 and 13 remain provisionally rejected under the judicially created doctrine of obviousness over co-pending applications 09/817,913 and 10/145,493. Applicants will overcome this rejection by terminal disclaimer once the present application is found to otherwise be allowable.

If the Examiner believes that any discussion of this communication would be helpful, the undersigned attorney can be reached by telephone at 781-933-6630.

Respectfully submitted,

Dated: 5/13/04



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